IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION OF	Confirmation No.: 5040
Engel *et al.*	Group Art Unit: 1617
Application No.: 09/523,455	Examiner: Carter, Kendra D.
Filed: March 10, 2000	

Title: Method for a Programmed Controlled Ovarian Stimulation Protocol

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF CONFERENCE REQUEST FOR REVIEW

In reply to the Final Office Action mailed January 4, 2011, Applicants submit the following Amendment and Remarks. A Notice of Appeal was filed May 9, 2011. This response is timely filed on or before August 9, 2011, with a one-month extension of time.

Claims 4-9 and 16-28 are pending. The Final Office Action contained three separate rejections under 35 U.S.C. §103(a), each of which relies on the teaches of *Felberbaum* et al. (1997) or *Olivennes* et al. (1994), in view of *Ziegler* et al. (1998), and further in view of *Hall* et al. (1991). These rejections are refuted for the reasons provided herein.

A. Claims 4, 5, 7, 16, 18, 21, and 25-28 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable in view of *Felberbaum* et al. (1997) or *Olivennes* et al. (1994), in view of *Ziegler* et al. (1998), and further in view of *Hall* et al. (1991).

Felberbaum is relied on for the teaching that second generation GnRH antagonists (*i.e.* Cetrorelix and Ganirelix) can be administered in an IVF program to avoid premature LH-surges, an improvement over first generation GnRH antagonists. The IVF program taught in *Felberbaum* involves stimulation with human menopausal gonadotropin (HMG) started on cycle day 2, then from day 7 until induction of ovulation by human chorionic gonadotrophin (hCG),

Cetrorelix is administered in daily fashion. *Felberbaum* does not disclose administering an LHRH antagoinist (*e.g.*,Cetrorelix) during the luteal phase of a first menstrual cycle, as is acknowledged by the Examiner of page 5 of the Final Office Action.

Regarding *Olivennes*, the Examiner explains on pages 4 and 5 of the Final Office Action that *Olivennes* teaches an IVF program having the same steps of *Felberbaum*. Thus, *Olivennes* also does not disclose administering an LHRH antagoinist (*e.g.*,Cetrorelix) during the luteal phase of a first menstrual cycle, as is acknowledged by the Examiner of page 5 of the Final Office Action..

Ziegler discloses an IVF program that does not use LHRH antagonists (*e.g.,* Cetrorelix and Ganirelix). Rather, *Ziegler* teaches the administration of Oestradiol to permit an advanced timing of the onset of controlled ovarian hyperstimulation treatments. See *e.g.*, *Ziegler* at Abstract. Oestradiol, however, is an LHRH antagonist. Thus, *Ziegler* fails to teach administering an LHRH antagonist (*e.g.*,Cetrorelix) during the luteal phase of a first menstrual cycle as recited in the present claims.

Further, *Ziegler* relates to an IVF program where the desired outcome to "synchronize the increase in endogenous FSH with the onset of HMG treatment." *Ziegler* at Abstract. *Ziegler* explains that in COH, "exogenous gonadotrophins are administered to amplify and sustain the gonadotrophic stimulus in order to prevent single follicular dominance by rescuing the rest of the cohort of follicles from atresia and hence achieve multiple ovulation." *Ziegler* at page 561, right column. In this manner, *Ziegler* promotes this approach as an alternative to the use of GnRH agonists. See *e.g.*, *Ziegler* at page 563, left coumn (stating that "[o]ur present protocol in which the timing of intercycle increase in FSH is controlled with physiological amounts of oestradiol… provides the same practical advantages without the complexity, the cost and the increased risk of ovarian hyper stimulation inherent to the use of GnRH agonists."). Accordingly, *Ziegler* is unrelated to the use of GnRH antagonists and fails to cure the deficiencies of *Felberbaum* and *Olivennes*. The combination of *Felberbaum* or *Olivennes* with *Ziegler* do not teach or suggest the administration of an LHRH antagonist during the luteal phase of a first menstrual cycle as recited in the present claims.

Hall is not related to an IVF program and does not cure the deficiencies of *Felberbaum*, *Olivennes* and *Ziegler*. *Hall* merely discloses the results of experiment designed to test examine the differential sensitivity of the ovary to temporary withdrawal of gonadotropin support at different stages of folliculogenesis and corpus luteum function. See *Hall* at Abstract. *Hall* shows that the developing ovarian follicle varies in its tolerance to gonadotropin withdrawal, and the dominant follicle becomes increasingly controlled by local factors during late follicular phase and more resistant to short-term gonadotropin deprivation. With regard to the luteal phase, *Hall* concludes that a 72-hour GnHR receptor blockade is not tolerated by the corpus luteum and results in luteolysis.

Hall dose not disclose the use of GnRH antagonists in an IVF program. *Hall* teaches that administration of GnRH antagonists can result in luteolysis. However, none of *Hall, Felberbaum*, *Olivennes*, or *Ziegler* teach or suggest inducing luteolysis as part of an IVF program. Further, none of *Hall, Felberbaum*, *Olivennes*, or *Ziegler* teach or suggest the need to induce luteolysis as part of an IVF program. Thus, the combination of *Felberbaum* or *Olivennes* with *Ziegler* and *Hall* does not achieve the method of the present claims.

The Office Action is thus absent a reasonable rationale or motivation to combine *Felberbaum* or *Olivennes* with *Ziegler* and *Hall* to achieve the method of the present claims. There is no rationale set forth by the Office as to why a person of ordinary skill in the art would modify the teachings of the cited references to arrive an IVF program that involves administering a LHRH antagonist during the luteal phase of a first menstrual cycle to induce luteal regression. The conclusions reached by the examiner merely allege that *Ziegler* teaches the desirability of "administering a composition during the luteal phase of one period and to allow for advanced scheduling of treatments to the next period." Office Action at page 6. Under this rationale, the administration of any composition in the luteal phase would have been obvious. This rationale is conclusory and improper. There is no scientific explanation or reasonable rationale set forth to support the desirability to substitute the administration of oestradiol, as disclosed in *Ziegler*, with an a LHRH antagonist. In view of the above, Applicants respectfully submit that the Examiner has failed to clearly articulate a reasonable rationale for supporting the rejections set forth under 35 U.S.C. §103(a).

B. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Felberbaum* et al. (of record) or *Olivennes* et al (of record), in view of (ii) *Ziegler* et al. (of record), and further in view of (iii) *Hall* et al. (of record), and further in view of *Garfield* et al (of record).

The inapplicability of *Felberbaum*, *Olivennes*, *Ziegler*, and *Hall* was discussed above. The Examiner cites *Garfield* as teaching clomiphene as a non-steroidal anti-estrogen. However, the present invention relates to LHRH antagonists not to estrogens or to anti-estrogens. Moreover, *Garfield* does not relate to the missing teaching, the administration of an LHRH antagonist during a first luteal phase to induce the timing of a second menstrual cycle. Accordingly, *Garfield* fails to cure the deficiencies of *Felberbaum*, or *Olivennes*, in view of *Ziegler* and *Hall*.

C. Claims 6, 8, 9,17,19, 20 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over (i) the article by *Felberbaum* et al. (of record) or *Olivennes* et al (of record), in view of (ii) *Ziegler* et al. (of record), and further in view of (iii) *Hall* et al. (of record), and further in view of (iv) *Deghengi* et al (of record) or *Rabasseda* et al (of record.).

The inapplicability of *Felberbaum*, *Olivennes*, *Ziegler*, and *Hall* was discussed above. The Examiner cites *Dehgenghi* and *Rabasseda* are cited as teaching specific LHRH antagonists. However, neither *Dehgenghi* nor *Rabasseda* relate to the missing teaching, the administration of an LHRH antagonist during a first luteal phase to induce the timing of a second menstrual cycle. Accordingly, *Dehgenghi* and *Rabasseda* fail to cure the deficiencies of *Felberbaum*, or *Olivennes*, in view of *Ziegler* and *Hall*.

Judicially Created Doctrine of Obviousness Double Patenting.

Claims 1 and 4-9, 16-21, and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,319,192 of *Engel* et al., in view of *Ziegler* et al., *Hall* et al., *Deghengi* , *Rabasseda*, and *Kent*,

as applied above. A terminal disclaimer was filed May 9, 2011, which should obviate this rejection.

CONCLUSION

An indication of allowance of all claims is solicited. Please charge any fees or credit any overpayments associated with the submission of this response to Deposit Account Number 03-3975.

Respectfully submitted,

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